Claims

1. A process for the isolation and purification of HMG-CoA reductase inhibitors from a mycelium biomass which comprises:
- clarifying a mycelium broth and concentrating the clarified broth to a lower volume,
- acidifying of the concentrate to a pH value in the range of 4.5 to 7.5, followed by extracting the HMG-CoA reductase inhibitor with ethyl acetate,
- optionally performing lactonization,
- crystallization of the HMG-CoA reductase inhibitor from a water-miscible or water-soluble organic solvent, and
- crystallization of the HMG-CoA reductase inhibitor from an organic solvent having limited miscibility or solubility with water.

2. The process according to claim 1, further comprising, before clarifying the mycelium biomass broth, the steps of dissolvating the HMG-CoA reductase inhibitor from a mycelium biomass at pH value between 9.5 and 13 into fermentation liquor, and adjusting the broth to a pH value between 7.5 and 8.5.

3. The process according to claim 2, wherein the dissolvation step is carried out at a temperature in the range of 10 to 40°C for less than one hour.

4. The process according to any one of the preceding claims, wherein clarifying the mycelium broth is carried out by removing the mycelium from the broth by means of filtration.

5. The process according to any one of the preceding claims, wherein said clarified broth is concentrated by means of reverse osmosis.

6. The process according to any one of the preceding claims, wherein the concentrate is acidified to a pH value in the range of 5.5 to 7.5.

7. The process according to claim 6, wherein the concentrate is acidified to a pH value in the range of 6.0 to 7.0.

8. The process according to any one of the preceding claims, wherein the HMG-CoA reductase inhibitor which is extracted from ethyl acetate and optionally lactonized is subjected to a purification step by adsorption chromatography.

9. The process according to claim 8, wherein a mixture of acetonitrile and water is used as the mobile phase for adsorption chromatography.

10. The process according to any one of the preceding claims, wherein the order of the crystallization steps is reversed.

11. The process according to any one of the preceding claims, wherein the water-miscible or water-soluble organic solvent used in the crystallization step is acetone or a low alkyl alcohol.

12. The process according to claim 11, wherein the crystallization step comprises dissolving the HMG-CoA reductase inhibitor in acetone, and then adding water thereto.

13. The process according to any one of the preceding claims, wherein the crystallization step from an organic solvent having limited miscibility or solubility with water comprises dissolving the HMG-CoA reductase inhibitor in said organic solvent at a concentration of 10 to 35 g/l, and removing one-third to three-fourth of said organic solvent.

14. The process according to any one of the preceding claims, wherein the organic solvent having limited miscibility or

solubility with water used in the crystallization step is ethyl acetate.

15. The process according to any one of the preceding claims, wherein HMG-CoA reductase inhibitors are obtained having a purity higher than 99.6%.

16. The process according to any one of the preceding claims, wherein the HMG-CoA reductase inhibitor is selected to be lovastatin.

17. A process for the purification of HMG-CoA reductase inhibitors which comprises subjecting the HMG-CoA reductase inhibitor to combined crystallization steps, which comprises crystallization from an water-miscible or water-soluble and crystallization from an organic solvent having limited miscibility or solubility with water, as final polishing steps to obtain HMG-CoA reductase inhibitors having a purity higher than 99.6%.

18. The process according to claim 17, wherein the obtained HMG-CoA reductase inhibitors have purity higher than 99.7 %.

19. The process according to claim 1 or 18, wherein wherein acetone or a low alkyl alcohol is used as the water-miscible or water-soluble organic solvent.

20. The process according to claim 19, wherein said crystallization comprises dissolving the HMG-CoA reductase inhibitor in acetone, and then adding water thereto.

21. The process according to any one of claims 17 to 20, wherein said crystallization from said organic solvent having limited miscibility or solubility with water comprises dissolving the HMG-CoA reductase inhibitor in said organic solvent at a concentration of 10 to 35 g/l, and removing one-third to three-fourth of said organic solvent.

22. The process according to any one of claims 17 to 21, wherein ethyl acetate is used as the organic solvent having limited miscibility or solubility with water.

23. Use of a process according to claim 1 or a process according to claim 17 for the isolation and/or purification of lovastatin.